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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,585	DONKENA ET AL.	
	Examiner	Art Unit	
	TERESA E. STRZELECKA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57,63-65 and 67-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-57,63-65 and 67-70* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Groups 1-15, claim(s) 1-8, drawn to a method for detecting or distinguishing between prostate cells proliferative disorders by obtaining a biological sample, determining expression level of at least one gene selected from the group consisting of ZNF185, PSP94, BPAG1, SORBS1, C21orf63, SVIL, PRIMA1, FLJ14084, TUA3, KIAA1210, SOX4, MLP, FABP5, MAL2 and Erg-2 or sequences that hybridize thereto.

If group 1 is elected, it corresponds to gene ZNF185, if group 2 is elected, it corresponds to gene PSP94, etc.

Group 16-30, claim(s) 9-15, 70, drawn to a method for detecting or distinguishing between prostate cells proliferative disorders by obtaining a biological sample; contacting genomic DNA with a reagent that distinguishes between methylated and unmethylated CpG dinucleotides within a target DNA which comprises at least 16 contiguous nucleotides of a sequence selected from the group consisting of SEQ ID NO: 1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51 and complements thereof.

If group 16 is elected, it corresponds to SEQ ID NO: 1, if group 17 is elected, it corresponds to SEQ ID NO: 29, etc.

Group 31-45, claim(s) 16-25, 70, drawn to a method for detecting or distinguishing between prostate cells proliferative disorders by obtaining a biological sample; contacting genomic DNA with a reagent that distinguishes between methylated and unmethylated CpG dinucleotides within a target DNA which comprises at least 16 contiguous nucleotides of a sequence selected from the group consisting of SEQ ID NO: 1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51 and complements thereof; determining the methylation state of at least one target CpG dinucleotide.

If group 31 is elected, it corresponds to SEQ ID NO: 1, if group 32 is elected, it corresponds to SEQ ID NO: 29, etc.

Group 46-60, claim(s) 26-45, 70, drawn to a method for detecting or distinguishing between prostate cells proliferative disorders by obtaining a biological sample; extracting the genomic DNA; treating genomic DNA with a reagent that converts unmethylated cytosines to uracil or

another base; contacting the treated DNA with an amplification enzyme and two primers which comprise at least 9 contiguous nucleotides complementary to a sequence selected from the group consisting of SEQ ID NO: 1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51 and complements thereof; determining the methylation state of at least one target CpG dinucleotide of a sequence selected from the group consisting of SEQ ID NO: 1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51 and complements thereof.

If group 46 is elected, it corresponds to SEQ ID NO: 1, if group 47 is elected, it corresponds to SEQ ID NO: 29, etc.

Group 61-75, claim(s) 46-50, 70, drawn to a method for detecting or distinguishing between prostate cells proliferative disorders by obtaining a biological sample; extracting the genomic DNA; treating genomic DNA comprising at least 16 contiguous nucleotides of a sequence selected from the group consisting of SEQ ID NO: 1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51 and complements thereof with a methylation-sensitive enzyme to cleave the DNA; determining the methylation state of at least one target CpG dinucleotide of a sequence selected from the group consisting of SEQ ID NO: 1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51 and complements thereof..

If group 61 is elected, it corresponds to SEQ ID NO: 1, if group 62 is elected, it corresponds to SEQ ID NO: 29, etc.

Group 76-90, claim(s) 51-57, 64, 65, 67-69, drawn to DNA comprising at least 16 contiguous nucleotides of a sequence selected from the group consisting of SEQ ID NO: 1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51 and complements thereof treated to convert unmethylated cytosines to uracil or another base.

If group 76 is elected, it corresponds to SEQ ID NO: 1, if group 77 is elected, it corresponds to SEQ ID NO: 29, etc.

Group 91-105, claim(s) 63, drawn to a method of manufacturing a nucleic acid array comprising at least one of attachment of an oligomer acoording to claim 55 or 56 or attachment of a set of oligomers according to claim 57 to a solid phase.

If group 91 is elected, it corresponds to SEQ ID NO: 1, if group 92 is elected, it corresponds to SEQ ID NO: 29, etc.

The inventions listed as Groups 1-105 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: GenBank sequence with accession No. Y09538 is 100% identical to bp 1-199 of SEQ ID NO: 1 and contains at least 9 contiguous nucleotides or at least 16 contiguous nucleotides of SEQ ID NO: 1 between CpG islands, e.g., nucleotides 1-46 of the sequence, therefore, Applicants' claims do not have a contribution over prior art.

2. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Groups 1-15

Species of expression level detection

A) presence, absence or mRNA level detected (claim 2),

B) presence, absence or polypeptide level detected (claim 3),

C) detecting the presence or absence of CpG methylation (claims 7, 8).

Species type of expression detected

D) decrease in expression of at least one gene (claim 4),

E) increase in expression of at least one gene (claim 5).

Groups 16-30

Species of types of tissues or disorders being distinguished

A) normal, non-prostate cell proliferative disorders, or adjacent benign tissues are distinguished from at least one condition selected from the group consisting of: intermediate, T2, Gleason score 6 lymph node positive and negative; high grade,T3, Gleason score 9 lymph node positive and negative; prostatic adenocarcinoma; and metastatic tumors (claim 10),

B) adjacent benign tissue is distinguished from at least one condition selected from the group consisting of: intermediate, T2, Gleason score 6 lymph node positive and negative; high grade,T3, Gleason score 9 lymph node positive and negative; prostatic adenocarcinoma; and metastatic tumors (claims 11-13),

C) tissues originating from the prostate are distinguished from tissues of non-prostate origin (claim 14),

D) prostate cell proliferative disorders are distinguished from healthy tissues (claim 15).

Groups 31-45

Species of distinguishing between methylated and non-methylated CpG dinucleotides

A) distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence comprises converting unmethylated cytosine bases within the target sequence to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties (claim 18),

B) distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence(s) comprises methylation state-dependent conversion or non-conversion of at least one CpG dinucleotide sequence to the corresponding converted or non-converted dinucleotide sequence (claim 19),

C) distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence comprises use of at least one nucleic acid molecule or peptide nucleic acid (PNA) molecule comprising, in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof (claims 21-25).

Groups 46-60

Species of contacting or amplifying

A) contacting or amplifying comprises use of at least one method selected from the group consisting of: use of a heat-resistant DNA polymerase as the amplification enzyme; use of a polymerase lacking 5'-3' exonuclease activity; use of a polymerase chain reaction (PCR); generation of a amplificate nucleic acid molecule carrying a detectable labels; and combinations thereof (claims 28, 29),

B) for the step of contacting the treated genomic DNA, the use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized (claims 31-35),

C) contacting or amplifying comprises use of methylation-specific primers (claim 41),

D) for the contacting step, using primer oligonucleotides comprising one or more CpG; TpG or CpA dinucleotides; and further comprising, for the determining step, the use of at least one method selected from the group consisting of: hybridizing in at least one nucleic acid molecule or peptide nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof; hybridizing at least one nucleic acid molecule that is bound to a solid phase and comprises a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes

under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof, hybridizing at least one nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof, and extending at least one such hybridized nucleic acid molecule by at least one nucleotide base; and sequencing, in the determining step, of the amplificate (claim 42),

E) for the contacting step, use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized; and further comprising, in the determining step, the use of at least one method selected from the group consisting of: hybridizing in at least one nucleic acid molecule or peptide nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof; hybridizing at least one nucleic acid molecule that is bound to a solid phase and comprises a contiguous sequence at least

9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof, hybridizing at least one nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof, and extending at least one such hybridized nucleic acid molecule by at least one nucleotide base; and sequencing, in the determining step, of the amplificate (claim 43),

F) in the contacting step, amplification by primer oligonucleotides comprising one or more CpG; TpG or CpA dinucleotides and further comprising, in the determining step, hybridizing at least one detectably labeled nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38,40, 42, 43, 45, 47, 49, 51, and complements thereof (claim 44),

G) in the contacting step, the use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which

it is hybridized, and further comprising, in the determining step, hybridizing at least one detectably labeled nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under stringent conditions to a bisulfite-converted sequence derived from a sequence selected from the group consisting of SEQ ID NOS:1, 29, 31, 32, 34, 35, 37, 38, 40, 42, 43, 45, 47, 49, 51, and complements thereof (claim 45).

Applicant is required, in reply to this action, to elect a single species from each set of species within a group to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The following claim(s) are generic: 1, 9, 16, 26.

3. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: they represent methods which use different method steps and materials.

4. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

6. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102,

103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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